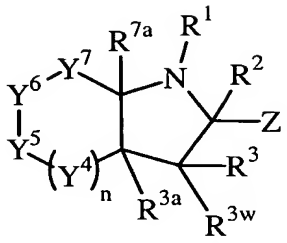
CLAIMS

What is claimed is:

1. A compound of Formula I



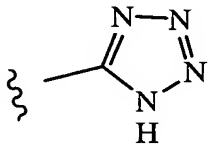
I

or a pharmaceutically acceptable salt thereof,

wherein:

Z is selected from COOH, $C(O)N(H)R^9$, and Z^1;

Z^1 is selected from: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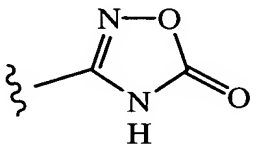
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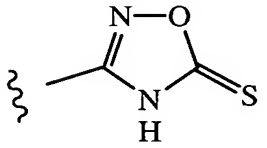
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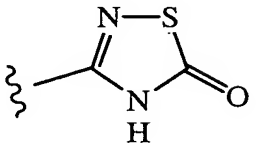
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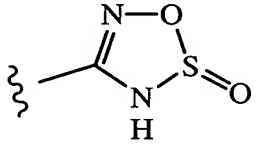

;

Each Y^4, Y^5, Y^6, and Y^7 is $C(R^{10})R^{10w}$; or

One of Y^4, Y^5, Y^6, and Y^7 is selected from O, S, S(O), $S(O)_2$, and NR^5, and the other three of Y^4, Y^5, Y^6, and Y^7 are each $C(R^{10})R^{10w}$; or

Two nonadjacent Y^4, Y^5, Y^6, and Y^7 are independently selected from O, S, S(O), $S(O)_2$, and NR^5, and the other two of Y^4, Y^5, Y^6, and Y^7 are each $C(R^{10})R^{10w}$;

Each R^2, R^3, R^{3w}, R^{3a}, R^{7a}, R^{10}, and R^{10w} is independently selected from: H, HO, H_2N, $H_2NS(O)_2$-$(G)_m$, HS, Halo, CN, CF_3, $FC(H)_2O$, $F_2C(H)O$, CF_3O, and

a group, which may be unsubstituted or substituted, independently selected from:

C_1-C_6 alkyl-$(G)_m$–,

C_2-C_6 alkenyl-$(G)_m$–,

C_2-C_6 alkynyl-$(G)_m$–,

2- to 6-membered heteroalkyl-$(G)_m$–,

2- to 6-membered heteroalkenyl-$(G)_m$–,

C_3-C_7 cycloalkyl-$(G)_m$–,

C_3-C_7 cycloalkenyl-$(G)_m$–,

C_7-C_{10} bicycloalkyl-$(G)_m$–,

3- to 7-membered heterocycloalkyl-$(G)_m$–,

7- to 10-membered heterobicycloalkyl-$(G)_m$–,

Phenyl-$(G)_m$–,

Naphthyl-$(G)_m$–,

5- and 6-membered heteroaryl-$(G)_m$–,

8- to 10-membered heterobiaryl-$(G)_m$–, and

any of the above R^2, R^3, R^{3w}, R^{3a}, R^{7a}, R^{10}, and R^{10w} groups each independently substituted on carbon or nitrogen atoms with from 1 to 6 substituents R^X;

wherein R^3 and R^{3w}, and any geminal pair of R^{10} and R^{10w}, and any two R^X substituents geminally substituted on a carbon atom in substituted R^2, R^3, R^{3w}, R^{3a}, R^{7a}, R^{10}, and R^{10w} groups further may independently be taken together with a carbon atom to which they are both bonded to form the group C(=O);

Each R^5 and R^9 is independently H, HO, or a group, which may be unsubstituted or substituted, independently selected from:

C_1-C_6 alkyl-$(L)_m$–,

C_2-C_6 alkenyl-$(L)_m$–,

C_2-C_6 alkynyl-$(L)_m$–,

2- to 6-membered heteroalkyl-$(L)_m$–,

2- to 6-membered heteroalkenyl-$(L)_m$–,

C_3-C_7 cycloalkyl-$(L)_m$–,

C_3-C_7 cycloalkenyl-$(L)_m$–,

C_7-C_{10} bicycloalkyl-$(L)_m$–,

3- to 7-membered heterocycloalkyl-$(L)_m$–,

7- to 10-membered heterobicycloalkyl-$(L)_m$–,

Phenyl-$(L)_m$–,

Naphthyl-$(L)_m$–,

5- and 6-membered heteroaryl-$(L)_m$–,

8- to 10-membered heterobiaryl-$(L)_m$–, and

any of the above R^5 and R^9 groups independently substituted, on carbon or nitrogen atoms, with from 1 to 6 substituents R^X;

R^1 is HO or a group that may be unsubstituted or substituted, independently selected from:

C_1-C_6 alkyl-$(T)_m$–,

C_2-C_6 alkenyl-$(T)_m$–,

C_2-C_6 alkynyl-$(T)_m$–,

2- to 6-membered heteroalkyl-$(T)_m$–,

2- to 6-membered heteroalkenyl-$(T)_m$–,

C_3-C_7 cycloalkyl-$(T)_m$–,

C_3-C_7 cycloalkenyl-$(T)_m$–,

C_7-C_{10} bicycloalkyl-$(T)_m$–,

3- to 7-membered heterocycloalkyl-$(T)_m$–,

7- to 10-membered heterobicycloalkyl-$(T)_m$–,

Phenyl-$(T)_m$–,

Naphthyl-$(T)_m$–,

5- and 6-membered heteroaryl-$(T)_m$–,

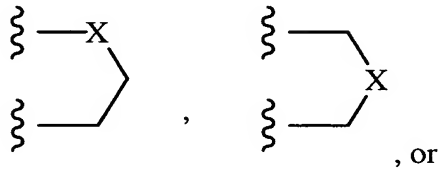
8- to 10-membered heterobiaryl-$(T)_m$–, and

any of the above R^1 groups independently substituted on a carbon or nitrogen atom, with from 1 to 6 substituents R^X;

R^1 may further be H when: (i) at least one of R^2, R^3, R^{3w}, R^{3a}, R^{7a}, R^{10}, and R^{10w} is not H, or (ii) Z is $C(O)N(H)R^9$ wherein R^9 is as defined above wherein m is 1 and L is $S(O)_2$, or (iv) Z is Z^1;

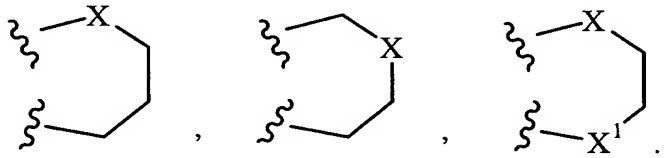
wherein any 2 groups each selected from R^5, R^{10}, and R^{10w} that are bonded to contiguous carbon or nitrogen atoms in Formula I may be taken together with the contiguous atoms in Formula I to which they are bonded to form C=C or C=N;

wherein any 2 groups selected from R^1, R^2, R^3, R^{3w}, R^{3a}, R^5, R^{7a}, R^{10}, and R^{10w} that are bonded to contiguous carbon or nitrogen atoms in Formula I may be taken together to form (i) a CH_2 diradical, (ii) a 3-membered diradical selected from:



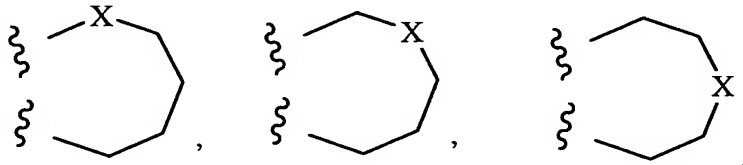
, or

(iii) a 4-membered diradical selected from:

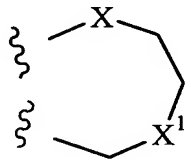


;

wherein any two groups R^3 and R^{3w}, and R^{10} and R^{10w}, that are geminally bonded to a single carbon atom in Formula I may be taken together to form a 4-membered diradical as defined above or a 5-membered diradical selected from:



, and



;

X is O, S, S(O), $S(O)_2$, or N-R;

X^1 is O or N-R;

Each G is independently selected from C(=O), S(O), $S(O)_2$, OC(O), $N(R^4)C(O)$, $(C_1\text{-}C_8$ alkylenyl$)_m$, (2- to 8-membered heteroalkylenyl$)_m$, and $(C_1\text{-}C_8$ alkylenyl$)_m$ and (2- to 8-membered heteroalkylenyl$)_m$ independently substituted on carbon or nitrogen atoms with from 1 to 4 substituents R^X;

Each T is independently selected from S(O), $S(O)_2$, $N(R^4)C(O)$, (C_1-C_8 alkylenyl)$_m$, (2- to 8-membered heteroalkylenyl)$_m$, and (C_1-C_8 alkylenyl)$_m$ and (2- to 8-membered heteroalkylenyl)$_m$ independently substituted on carbon or nitrogen atoms with from 1 to 4 substituents R^X;

Each L is independently selected from O, $N(R^4)$, S(O), $S(O)_2$, C(=O), C(O)O, OC(O), $C(O)N(R^4)$, $N(R^4)C(O)$, $OC(O)N(R^4)$, $N(R^4)C(O)O$, $N(R^4)C(O)N(R^{4w})$, (C_1-C_8 alkylenyl)$_m$, (2- to 8-membered heteroalkylenyl)$_m$, and (C_1-C_8 alkylenyl)$_m$ and (2- to 8-membered heteroalkylenyl)$_m$ independently substituted on carbon or nitrogen atoms with from 1 to 4 substituents R^X;

Each R, R^4, and R^{4w} is independently H or C_1-C_6 alkyl, which C_1-C_6 alkyl may be unsubstituted or substituted with from 1 to 3 substituents R^X;

Each R^X is independently selected from: HO, H_2N, $H_2NS(O)_2$, CN, CF_3, FCH_2O, $F_2C(H)O$, CF_3O, O_2N, C_1-C_6 alkyl-$(Q)_m$–, 2- to 6-membered heteroalkyl-$(Q)_m$–, C_3-C_7 cycloalkyl-$(Q)_m$–, 3- to 7-membered heterocycloalkyl-$(Q)_m$–, Phenyl-$(Q)_m$, and 5-membered heteroaryl-$(Q)_m$,

wherein phenyl and 5-membered heteroaryl-$(Q)_m$ each is unsubstituted or independently substituted with from 1 to 3 substituents selected from halo, HO, HOC(O), $CH_3OC(O)$, $CH_3C(O)$, H_2N, CF_3, CN, and C_1-C_6 alkyl;

wherein each R^X substituent on a carbon atom may further be independently selected from: HS, (C_1-C_6 alkyl)-S, halo, and HO_2C; and

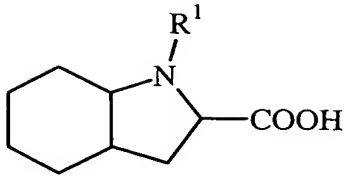
Each Q independently is O, $N(R^6)$, S(O), $S(O)_2$, C(=O), C(O)O, OC(O), $C(O)N(R^6)$, $N(R^6)C(O)$, $OC(O)N(R^6)$, $N(R^6)C(O)O$, or $N(R^6)C(O)N(R^{6w})$;

Each R^6 and R^{6w} independently is H or unsubstituted C_1-C_6 alkyl;

Each m independently is an integer of 0 or 1; and

Each n independently is an integer of from 0 to 2.

2. The compound according to Claim 1 of Formula II



II

or a pharmaceutically acceptable salt thereof,

wherein R^1 is HO or a group that may be unsubstituted or substituted, independently selected from:

C_1-C_6 alkyl-$(T)_m$–, C_2-C_6 alkenyl-$(T)_m$–, C_2-C_6 alkynyl-$(T)_m$–, 2- to 6-membered heteroalkyl-$(T)_m$–, 2- to 6-membered heteroalkenyl-$(T)_m$–, C_3-C_7 cycloalkyl-$(T)_m$–, C_3-C_7 cycloalkenyl-$(T)_m$–, C_7-C_{10} bicycloalkyl-$(T)_m$–, 3- to 7-membered heterocycloalkyl-$(T)_m$–, 7- to 10-membered heterobicycloalkyl-$(T)_m$–, Phenyl-$(T)_m$–, Naphthyl-$(T)_m$–, 5- and 6-membered heteroaryl-$(T)_m$–, 8- to 10-membered heterobiaryl-$(T)_m$–, and any of the above R^1 groups independently substituted on a carbon or nitrogen atom, with from 1 to 6 substituents R^X;

Each T is independently selected from S(O), $S(O)_2$, $N(R^4)C(O)$, (C_1-C_8 alkylenyl)$_m$, (2- to 8-membered heteroalkylenyl)$_m$, and (C_1-C_8 alkylenyl)$_m$ and (2- to 8-membered heteroalkylenyl)$_m$ independently substituted on carbon or nitrogen atoms with from 1 to 4 substituents R^X;

Each R^4 is independently H or C_1-C_6 alkyl, which C_1-C_6 alkyl may be unsubstituted or substituted with from 1 to 3 substituents R^X;

Each R^X is independently selected from: HO, H_2N, $H_2NS(O)_2$, CN, CF_3, FCH_2O, $F_2C(H)O$, CF_3O, O_2N, C_1-C_6 alkyl-$(Q)_m$–, 2- to 6-membered heteroalkyl-$(Q)_m$–, C_3-C_7 cycloalkyl-$(Q)_m$–, 3- to 7-membered heterocycloalkyl-$(Q)_m$–, Phenyl-$(Q)_m$, and 5-membered heteroaryl-$(Q)_m$,

wherein phenyl and 5-membered heteroaryl-$(Q)_m$ each is unsubstituted or independently substituted with from 1 to 3 substituents selected from halo, HO, HOC(O), $CH_3OC(O)$, $CH_3C(O)$, H_2N, CF_3, CN, and C_1-C_6 alkyl;

wherein each R^X substituent on a carbon atom may further be independently selected from: HS, (C_1-C_6 alkyl)-S, halo, and HO_2C; and

Each Q independently is O, $N(R^6)$, S(O), $S(O)_2$, C(=O), C(O)O, OC(O), $C(O)N(R^6)$, $N(R^6)C(O)$, $OC(O)N(R^6)$, $N(R^6)C(O)O$, or $N(R^6)C(O)N(R^{6w})$;

Each R^6 and R^{6w} independently is H or unsubstituted C_1-C_6 alkyl; and

Each m independently is an integer of 0 or 1.

3. The compound according to Claim 2, wherein R^1 is unsubstituted or substituted C_1-C_6 alkyl-$(L)_m$.

4. The compound according to Claim 1 selected from:

1-methyl-octahydroindole-2-carboxylic acid;

[2(S), 3a(S), 7a(S)]-1-methyl-octahydro-indole-2-carboxylic acid hydrochloride;

[2(S), 3a(S), 7a(S)]-1-methyl-octahydro-indole-2-carboxylic acid hemi tartaric acid salt;

[2(S), 3a(S), 7a(S)]-1-methyl-octahydro-indole-2-carboxylic acid;

1-(2-amino-1-oxopropyl)-octahydro-indole-2-carboxylic acid;

[2(S), 3a(S), 7a(S)]-1-ethyl-octahydro-indole-2-carboxylic acid;

[2(R), 3a(R), 7a(R)]-1-methyl-octahydro-indole-2-carboxylic acid.

5. The compound according to Claim 1, selected from:

(2R,3aS,7aS)-2-methyl-octahydroindole-2-carboxylic acid hydrochloride; and

(2S,3aS,7aS)-2-methyl-octahydroindole-2-carboxylic acid hydrochloride.

6. The compound according to Claim 1, selected from:

6–Ethyl–octahydro–indole–2–carboxylic acid hydrochloride;

(2S, 3aR, 6R/S, 7aR)-6–Phenyl–octahydro–indole–2–carboxylic acid;

6–Methoxy–octahydro–indole–2–carboxylic acid hydrochloride;

5–Ethyl–octahydro–indole–2–carboxylic acid hydrochloride;

5–Methyl–octahydro–indole–2–carboxylic acid hydrochloride;

5–Cyclohexylcarbonylamino–octahydro–indole–2–carboxylic acid hydrochloride;

5–Amino–octahydro–indole–2–carboxylic acid hydrochloride;
5–(1,1-Dimethylethyl)–octahydro–indole–2–carboxylic acid hydrochloride;
7–Methyl–octahydro–indole–2–carboxylic acid hydrochloride; and
4–Trifluoromethyl–octahydro–indole–2–carboxylic acid hydrochloride.

7. The compound according to Claim 1, selected from:
(2S, 3aS, 7aS)–N–(Octahydroindole–2–carbonyl)–methanesulfonamide;
(2S, 3aS, 7aS)–N–(1-Methyl-octahydroindole–2–carbonyl)–methanesulfonamide;
(2S, 3aS, 7aS)–N–(Octahydroindole–2–carbonyl)–trifluoromethanesulfonamide; and
(2S, 3aS, 7aS)–N–(1-Methyl-octahydroindole–2–carbonyl)–trifluoromethanesulfonamide; or
a pharmaceutically acceptable salt thereof.

8. The compound according to Claim 1, selected from:
(S,S,S)-3-(Octahydroindol-2-yl)-4H-[1,2,4]oxadiazol-5-one hydrochloride;
(S,S,S)-5-(Octahydroindol-2-yl)-1H-tetrazole.
(1aS,1bS,5aS,6aS)–octahydro–6–aza–cyclopropa[*a*]indene–6a–carboxylic acid; or
a pharmaceutically acceptable salt thereof.

9. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, or excipient.

10. A pharmaceutical composition, comprising a compound according to Claim 2, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, or excipient.

11. A method of treating joint cartilage damage, osteoarthritis, rheumatoid arthritis, or joint inflammation, or alleviating joint pain, in a mammal

suffering from joint cartilage damage, osteoarthritis, rheumatoid arthritis, joint inflammation, or joint pain, respectively, comprising administering to the mammal a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

12. A method of treating joint cartilage damage, osteoarthritis, rheumatoid arthritis, or joint inflammation, or alleviating joint pain, in a mammal suffering from joint cartilage damage, osteoarthritis, rheumatoid arthritis, joint inflammation, or joint pain, respectively, comprising administering to the mammal a compound according to Claim 2, or a pharmaceutically acceptable salt thereof.